Claims

1. A targetable diagnostic and/or therapeutically active agent comprising a suspension in an aqueous carrier liquid of a reporter comprising gas-containing or gas-generating material, said agent being capable of forming at least two types of binding pairs with a target.

2. An agent as claimed in claim 1 wherein the gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium hexafluoride, a low molecular weight hydrocarbon, a ketone, an ester, a halogenated low molecular weight hydrocarbon or a mixture of any of the foregoing.

3. An agent as claimed in claim 2 wherein the gas comprises a perfluorinated ketone, perfluorinated ether or perfluorocarbon.

4. An agent as claimed in claim 2 wherein the gas comprises sulphur hexafluoride or a perfluoropropane, perfluorobutane or perfluoropentane.

5. An agent as claimed in any of the preceding claims comprising gas microbubbles stabilised by a coalescence-resistant surface membrane, a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.

6. An agent as claimed in claim 5 wherein said surfactant comprises at least one phospholipid.

7. An agent as claimed in claim 6 wherein at least 75% of the said surfactant material comprises phospholipid molecules individually bearing net overall charge.

8. An agent as claimed in claim 7 wherein at least 75% of the film-forming surfactant material comprises one or more phospholipids selected from phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins.

9. An agent as claimed in claim 8 wherein at least 80% of said phospholipids comprise phosphatidylserines.

10. An agent as claimed in any of the preceding claims wherein said gas-containing or gas-generating material is conjugated to at least two vectors or to one vector capable of binding to at least two binding sites.

11. An agent as claimed in any of claims 1 to 9 wherein said gas-containing or gas-generating material is conjugated to one or more targeting vectors having specificity for one or more cellular surface receptors and further comprises moieties capable of binding to a receptor system so as to induce a therapeutic response.

12. An agent as claimed in any of the preceding claims wherein the vector or vectors are selected from antibodies; cell adhesion molecules; cell adhesion molecule receptors; cytokines; growth factors; peptide hormones and pieces thereof; non-bioactive binders of receptors for cell adhesion molecules, cytokines, growth factors and peptide hormones; oligonucleotides and modified oligonucleotides; DNA-binding drugs; protease substrates/inhibitors; molecules generated from combinatorial libraries; small bioactive molecules; and proteins and peptides which bind to cell-surface proteoglycans.

13. An agent as claimed in any of the preceding claims wherein the vector or vectors have affinity for targets at a level such that the agent interacts with but does

not fixedly bind to said targets.

14. An agent as claimed in claim 13 wherein the vector or vectors are selected from ligands for cell adhesion proteins and cell adhesion proteins which have corresponding ligands on endothelial cell surfaces.

15. An agent as claimed in any of the preceding claims wherein the vector or vectors are sited such that they are not readily exposed to the target.

16. An agent as claimed in any of the preceding claims wherein the vector or vectors are coupled or linked to the reporter by means of avidin-biotin and/or streptavidin-biotin interactions.

17. An agent as claimed in any one of claims 1 to 15 wherein the vector or vectors may be covalently or non-covalently coupled or linked to the reporter.

18. An agent as claimed in any one of claims 1 to 15 wherein the vector is coupled or linked to the reporter by means of electrostatic charge interaction.

19. An agent as claimed in any of the preceding claims which further contains moieties which are radioactive or are effective as X-ray contrast agents, light imaging probes or spin labels.

20. An agent as claimed in any preceding claim further comprising a therapeutic compound.

21. An agent as claimed in claim 20 wherein said therapeutic compound is an antineoplastic agent, blood product, biological response modifier, antifungal agent, hormone or hormone analogue, vitamin, enzyme, antiallergic agent, tissue factor inhibitor, platelet

inhibitor, coagulation protein target inhibitor, fibrin formation inhibitor, fibrinolysis promoter, antiangiogenic, circulatory drug, metabolic potentiator, antitubercular, antiviral, vasodilator, antibiotic, antiinflammatory, antiprotozoan, antirheumatic, narcotic, opiate, cardiac glycoside, neuromuscular blocker, sedative, local anaesthetic, general anaesthetic or genetic material.

22. An agent as claimed in claims 20 or 21 wherein said therapeutic compound is covalently coupled or linked to the reporter through disulphide groups.

23. An agent as claimed in claim 20 or claim 21 wherein a lipophilic or lipophilically-derivatised therapeutic compound is linked to the reporter through hydrophobic interactions.

24. A combined formulation comprising:

i) a first administrable composition comprising a pre-targeting vector having affinity for a selected target; and

ii) a second administrable composition comprising an agent as claimed in any of the preceding claims, said agent comprising a vector having affinity for said pre-targeting vector.

25. A combined formulation as claimed in claim 24 wherein said pre-targeting vector comprises a monoclonal antibody.

26. A combined formulation comprising:

i) a first administrable composition comprising an agent an agent as claimed in any of claims 1 to 23, and

ii) a second administrable composition comprising a substance capable of displacing or releasing said

agent from its target.

27. A combined formulation comprising:

i) a first administrable composition comprising an agent as claimed in claim 22, and

ii) a second administrable composition comprising a reducing agent capable of reductively cleaving the disulphide groups coupling or linking the therapeutic compound and reporter in the agent of said first administrable composition.

28. A process for the preparation of a targetable diagnostic and/or therapeutically active agent as defined in claim 1 which comprises coupling or linking at least one vector to a reporter comprising gas-containing or gas-generating material such that said agent is capable of forming at least two types of binding pairs with a target.

29. A process as claimed in claim 28 wherein a therapeutic compound is also combined with the reporter.

30. Use of an agent as claimed in any of claims 1 to 23 as a targetable ultrasound contrast agent.

31. A method of generating enhanced images of a human or non-human animal body which comprises administering to said body an agent as claimed in any of claims 1 to 23 and generating an ultrasound, magnetic resonance, X-ray, radiographic or light image of at least a part of said body.

32. A method as claimed in claim 31 which comprises the steps:

i) administering to said body a pre-targeting vector having affinity for a selected target; and thereafter

ii) administering an agent as claimed in any of claims 1 to 23, said agent comprising a vector having affinity for said pre-targeting vector.

33. A method as claimed in claim 32 wherein said pre-targeting vector comprises a monoclonal antibody.

34. A method as claimed in claim 31 which comprises the steps:

i) administering to said body an agent as claimed in any of claims 1 to 23; and thereafter

ii) administering a substance capable of displacing or releasing said agent from its target.

35. A method as claimed in any of claims 31 to 34 wherein said agent further comprises a therapeutic compound.

36. A method as claimed in claim 35 wherein said therapeutic compound is covalently coupled or linked to the reporter through disulphide groups, and a composition comprising a reducing agent capable of reductively cleaving said disulphide groups is subsequently administered.

37. A method for *in vitro* investigation of targeting by an agent as defined in any of claims 1 to 23 wherein cells expressing a target are fixedly positioned in a flow chamber, a suspension of said agent in a carrier liquid is passed through said chamber, and binding of said agent to said cells is examined.

38. A method as claimed in claim 37 wherein the flow rate of carrier liquid is controlled to simulate shear rates encountered *in vivo*.